substantially racemic oxybutynin for the management of incontinence, wherein the method comprises administering a sustained-release dose of 5 mg to 30 mg of a member selected from the group consisting of oxybutynin and its pharmaceutically acceptable salt thereof up to twenty-four hours to increase the therapeutic index.

12. (Amended) A method for relaxing bladder muscles and for decreasing concomitantly dry-mouth in a patient administered substantially racemic oxybutynin hydrochloride, wherein the method comprises administering 5 mg to 30 mg of oxybutynin hydrochloride in a sustained-rate up to twenty-four hours to increase the therapeutic index.

13. (Cancelled)

14. (Amended) A method of manufacture of a sustained release dosage form indicated for oxybutynin therapy and for the management of dry mouth associated therewith, the manufacture comprising the step of incorporating substantially racemic oxybutynin into a sustained release dosage form, which when admitted daily into an environment of use releases oxybutynin to provide an increased therapeutic index.

REMARKS

Claims 1-14 are examined in the final Office Action dated 06/26/2002. Claims 1, 2, 4 and 7-14 are rejected under 35 U.S.C. §102(b) and claims 3, 5, 6 and 7-14 are rejected under 35 U.S.C. §103(a). These rejections are overcome by the above amendments and are otherwise traversed for the reasons discussed below.

Claims 1, 3, 5-12 and 14 have been amended to more particularly point out and claim Applicants' disclosed invention. Support for the amendments can be found

throughout the specification and claims as originally filed. Thus, no new matter has been added to the application by way of the amendment.

Rejections Under 35 U.S.C. § 102

Claims 1, 2, 4 are rejected under 35 U.S.C. §102(b) as being anticipated by *Baichwal* (US Pat. No. 5,399,359).

The Examiner asserts that the "desire of increasing the therapeutic index of oxybutynin is clearly inherent by the teachings of Baichwal." However, while *Baichwal* may inherently suggest that an increased therapeutic index is desired, *Baichwal* does not disclose the means to achieve this desire, much less to the extent achieved by Applicants' invention. Applicants disclose and claim the ability to increase the therapeutic index through the claimed invention.

In this regard, Applicants amend Claim 1 to point out and distinctly claim that the present invention is unaffected by meals. Additionally, Applicants amend Claim 1 to include that the present invention exhibits true sustained release by claiming a substantially zero order release rate to achieve the increase in the therapeutic index. Therefore, Claims 1, 2, and 4 are not anticipated by *Baichwal,* are patentable and are in condition for allowance and withdrawal of this rejection is respectfully requested.

Claims 7-14 are rejected under 35 U.S.C. §102(b) as anticipated by *Aberg et al* (US Pat. No. 5,532,278).

Applicants' amended claims denote enantomeric mixtures rather than the substantially (S)-oxybutynin composition taught by *Aberg* by claiming substantially racemic oxybutynin.

Accordingly, claims 1, 2, 4, and 7-14 are not anticipated by *Baichwal* and *Aberg* and withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C.§ 103(a)

Claims 3,5, and 6 stand rejected as being unpatentable over *Baichwal*.

The Examiner asserts that *Baichwal* motivates toward 24 hour therapy and teaches the use of a rate modifying ingredient, which is capable of slowing the release rate of the final product. *Baichwal* at Col. 5, lines 45-48.

This rejection is respectfully traversed because there is no teaching in *Baichwal* to motivate use of slower rates of release. *Baichwal* may identify an ingredient capable of slowing the release rate of the final product, however, *Baichwal* notably does not incorporate this ingredient into any formulations disclosed and does not identify that further slowing of the release rate to extend the duration of release is preferred. Indeed, by not showing slower releases or extended duration of releases, *Baichwal* motivates away from further slowing of the rate of release to increase the therapeutic index.

Applicants' claims particularly point out and claim an increase in the therapeutic index of oxybutynin through the present invention that is not obtained through *Baichwal*'s matrix formulation which releases at least about 50% of the oxybutynin within the first four hours after administration. Applicants' claimed invention releases oxybutynin at substantially zero order over an extended period of time to increase the therapeutic index while providing therapeutic blood plasma levels over 24 hours.

As such, *Baichwal* does not make Applicants' invention obvious as it does not teach or motivate toward slowing the rate of release to extend the duration of release of oxybutynin in order to increase the therapeutic index of oxybutynin. Therefore, Claims 3, 5 and 6 are not obvious in view of *Baichwal,* are patentable and are in condition for allowance and withdrawal of this rejection is respectfully requested.

Claims 7-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Aberg et al.* in view of *Baichwal*.

This rejection is respectfully traversed because *Aberg* teaches delivery of a particular enantiomer of oxybutynin to reduce side effects whereas Applicants' claims are to a controlled release of racemic oxybutynin to increase the therapeutic index, and

reduce side effects. The Examiner asserts that *Aberg* is relied upon for controlled delivery of (S)-oxybutynin and *Baichwal* for delivery over 24 hours. However, there is no motivation in either piece of art to deliver racemic oxybutynin at substantially zero order to reduce side affects and increase the therapeutic index as claimed by Applicants. Moreover, there is no teaching in either *Baichwal* or *Aberg* to increase the therapeutic index (reduce side effects) through zero order release.

As such, it would not have been *prima facie* obvious to a person of ordinary skill in the art at the time of the invention to prepare a controlled release dosage form utilizing racemic oxybutynin to increase the therapeutic index, and reduce side effects.

Accordingly, *Baichwal* and *Aberg* do not anticipate claims 7-14 and withdrawal of this rejection is respectfully requested to permit allowance.

CONCLUSION

For these reasons, Applicants assert that the rejection of Claims 1-12 and 14 is not appropriate and withdrawal of the rejections is respectfully solicited. Applicants respectfully submit that Claims 1-12 and 14 are patentable and are in a position for allowance.

Reconsideration of the application is respectfully requested. Please direct any questions to the undersigned attorney at (650) 564-5171.

The Commissioner is hereby authorized to charge any additional fees associated with this paper or during the pendency of this application, or credit any overpayment, to Deposit Account No. 01-1173.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Respectfully submitted,

Date: August 29, 2002

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Version with markings to show changes made

In the Claims:

1. (Amended) A sustained release dosage form comprising oxybutynin for use in managing the plasma concentration of oxybutynin and the dry mouth associated with [the] use of oxybutynin, wherein the sustained dosage form upon once daily administration is characterized by the substantially zero order sustained release unaffected by meals of a therapeutically effective dose of oxybutynin to provide an increased therapeutic index.

2. The sustained release dosage form according to claim 1, wherein the plasma concentration is proportional to the sustained release dose.

3. (Amended) The sustained release dosage form according to claim 1, wherein the sustained release dosage form releases up to 25 mg per hour of oxybutynin over about 24 hours, or therapeutically acceptable oxybutynin salt thereof.

4. The sustained release dosage form according to claim 1, wherein the sustained release dosage form comprises up to 650 mg of oxybutynin, or therapeutically acceptable oxybutynin salt thereof.

5. (Amended) A sustained release dosage form comprising oxybutynin and a pharmaceutically acceptable carrier for managing dry mouth associated with oxybutynin, wherein the sustained release dosage form upon once daily use is characterized by a sustained release therapeutically effective dose up to 25 mg per hour over about 24 hours to provide an increased therapeutic index.

6. (Amended) Oxybutynin for use in providing a sustained release dosage form comprising oxybutynin and a pharmaceutically acceptable carrier, wherein the sustained release dosage form contains up to 650 mg of oxybutynin and up to 450 mg of a pharmaceutically acceptable carrier for releasing up to 25 mg per hour of oxybutynin to provide an increased therapeutic index over about 24 hours.

7. (Amended) A method for managing dry-mouth in a patent administered substantially racemic oxybutynin, wherein the method comprises orally administering to the patient a sustained release dosage form comprising an oxybutynin selected from the group consisting of oxybutynin and its pharmaceutically acceptable salt thereof, that administers the oxybutynin at a controlled rate over twenty-four hours to provide an increased therapeutic index.

8. (Amended) A method for managing dry mouth in a patient administered substantially racemic oxybutynin for the management of incontinence, wherein the method comprises administering a sustained-release dose of 5 mg to 30 mg of a member selected from the group consisting of oxybutynin and its pharmaceutically acceptable salt thereof up to twenty-four hours to provide an increased therapeutic index.

9. (Amended) A method for relaxing bladder muscles and for managing concomitantly dry mouth in a patient administered substantially racemic oxybutynin hydrochloride, wherein the method comprises administering 5 mg to 30 mg of oxybutynin hydrochloride in a sustained rate up to twenty-four hours to provide an increased therapeutic index.

10. (Amended) A method for decreasing the incidence of dry-mouth in a patient administered substantially racemic oxybutynin, wherein the method comprises orally administering to the patient a sustained-release dosage form comprising an

oxybutynin selected from the group consisting of oxybutynin and its pharmaceutically acceptable salt thereof, that administers the oxybutynin in a controlled rate over twenty-four hours to provide an increased therapeutic index.

11. (Amended) A method for decreasing dry-mouth in a patient administered substantially racemic oxybutynin for the management of incontinence, wherein the method comprises administering a sustained-release dose of 5 mg to 30 mg of a member selected from the group consisting of oxybutynin and its pharmaceutically acceptable salt thereof up to twenty-four hours to increase the therapeutic index.

12. (Amended) A method for relaxing bladder muscles and for decreasing concomitantly dry-mouth in a patient administered substantially racemic oxybutynin hydrochloride, wherein the method comprises administering 5 mg to 30 mg of oxybutynin hydrochloride in a sustained-rate up to twenty-four hours to increase the therapeutic index.

13. (Cancelled)

14. (Amended) A method of manufacture of a sustained release dosage form indicated for oxybutynin therapy and for the management of dry mouth associated therewith, the manufacture comprising the step of incorporating substantially racemic oxybutynin into a sustained release dosage form, which when admitted daily into an environment of use releases oxybutynin to provide an increased therapeutic index.